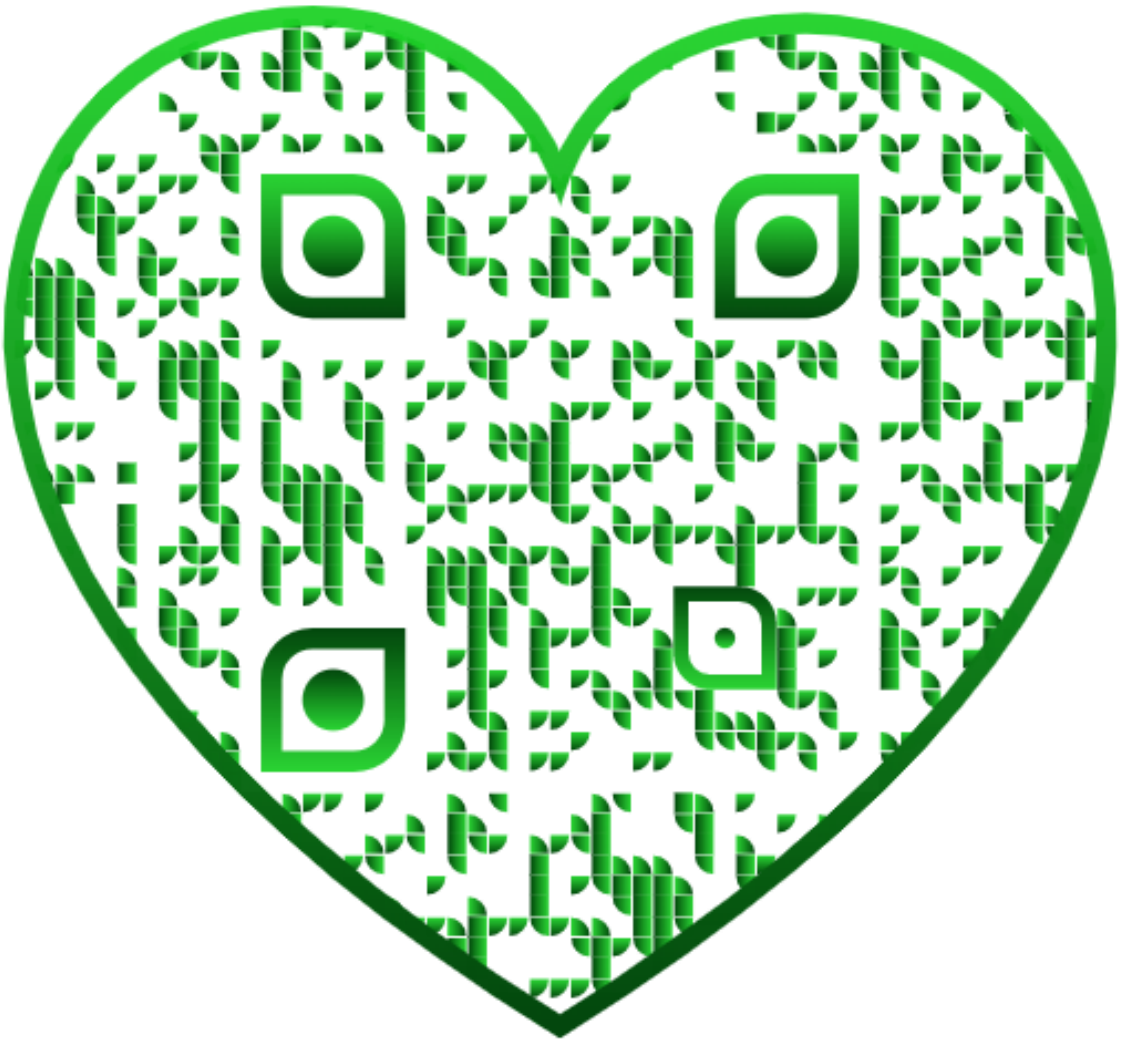
Pharmaceutics

Prof /Mahmoud Mahyoob Alburyhi
Professor of Pharmaceutics
and Industrial Pharmacy
Faculty of Pharmacy – Sana'a University

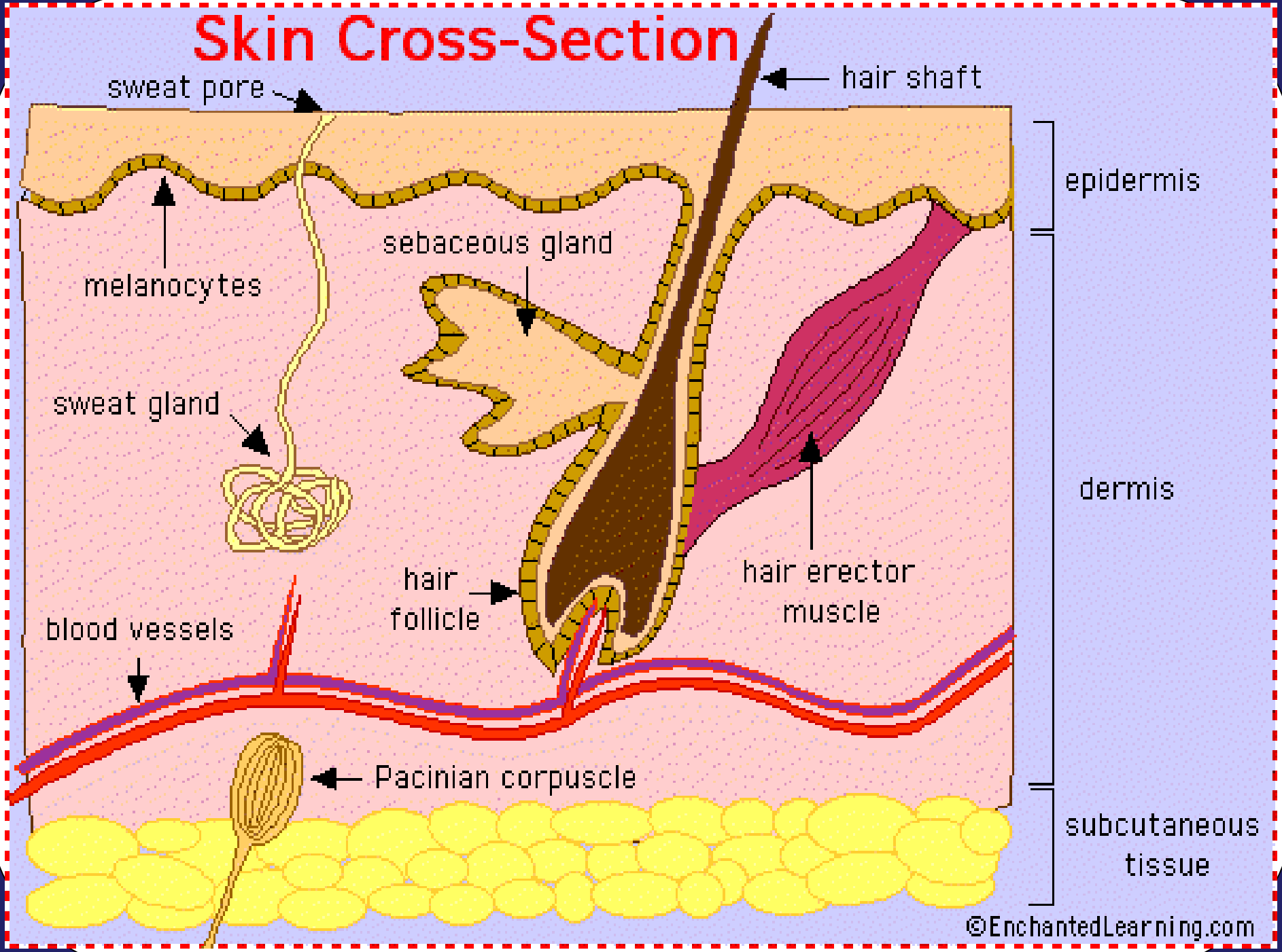


Semisolids

Dosage Forms

Skin anatomy & physiology

Skin Cross-Section



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The barrier function of the skin

The most extensive and readily accessible organ

- **Covers a surface area of approximately 2 m^2**
- **Receives about one-third of the blood circulation.**
- **Composed of three tissue layers:**
  - **Epidermis**
  - **Dermis**
  - **Subcutaneous fat tissue or hypodermis**

Skin layers: epidermis

The outer layer of skin, composed of stratified epithelial cells

– Consisted of two parts:

» The stratum corneum:

- **The outermost layer of the epidermis**
- **Responsible for the barrier function of skin**
- **Consisted of many layers of keratinized cells (keratinocytes)**
- **Replenished about every 2 weeks in mature adult**
- **Approximately 20% water content**
- **Thickness varies (palms and soles vs. surface of the trunk)**

Skin layers: epidermis
The stratum germinativum:

• **In the thicker parts of the skin, the transition from the living cells of the germinativum zone to the stratum corneum is made prominent by three layers:**

- **– The stratum spinosom**
- **– The stratum granulosum**
- **– Stratum lucidum**

– These layers are also responsible for regeneration and hydration of skin.

Dermis, subcutaneous tissue & appendages

Dermis:

- Functions of thermoregulation
- Supports the vascular network
- Supplies the avascular epidermis with nutrients
- The upper portion of the dermis contains blood vessels, lymphatics, and nerve endings

Dermis, subcutaneous tissue & appendages

Subcutaneous tissue:

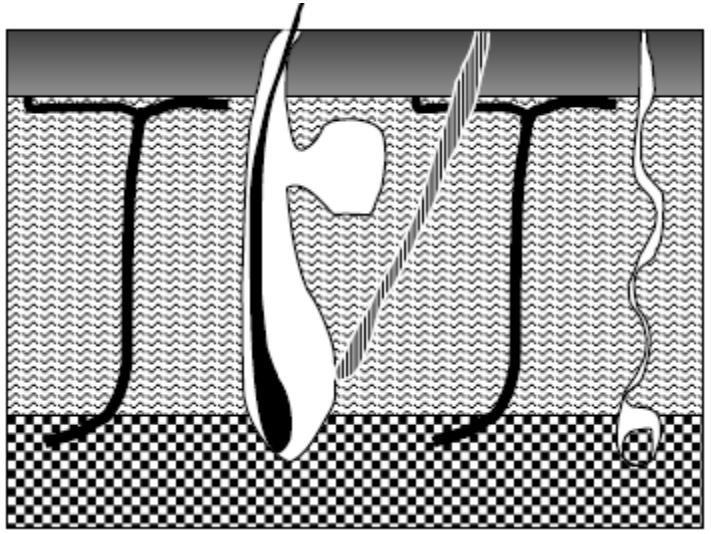
– Sheet of fat containing tissue attaching the dermis to the underlying structures

- **Skin appendages:**
  - – Hair follicles
  - – Sweat glands
  - – Sebaceous glands

Factors for Dosage Form Selection

Which Target Tissues?

- Skin surface
- Stratum corneum
- Viable epidermis
- Upper dermis
- Skin appendages
- Systemic absorption

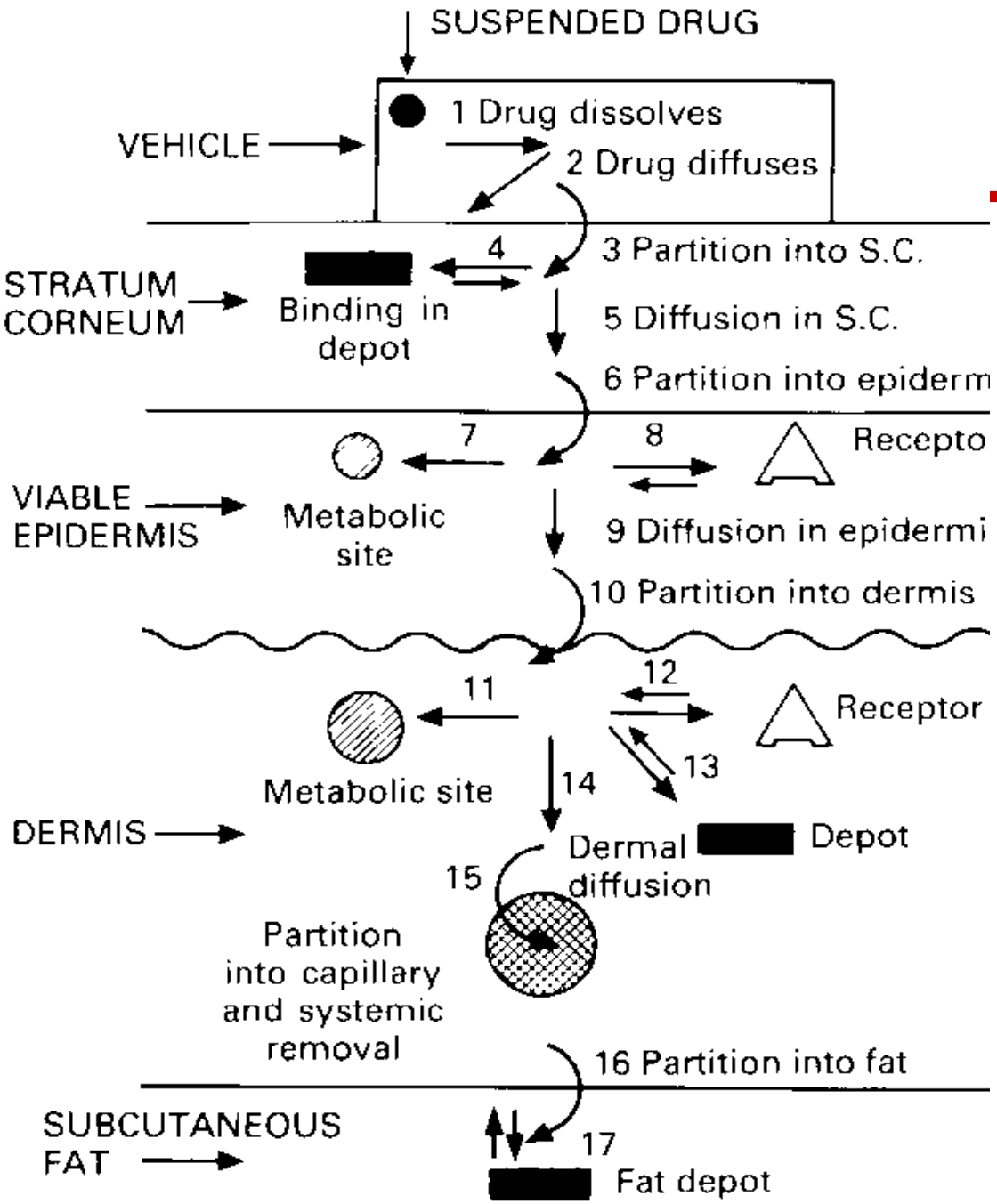


Target above or below stratum corneum?

- Above stratum corneum is easier target
  - – Absorption increased side effects
    - Example: insect repellent & sun screen
  - – Minimize percutaneous absorption
    - e.g., change partition coefficient
- Below stratum corneum is more difficult target
  - – Need --> Percutaneous Absorption
  - – Barrier function of Stratum Corneum limits penetration of drugs
  - – Formulate to cross Stratum corneum
  - – Transdermal patches --> systemic delivery
    - Control surface area --> dose
    - Example: nitroglycerin ointment vs patch

Example of Medicaments Prescribed For Semisolids

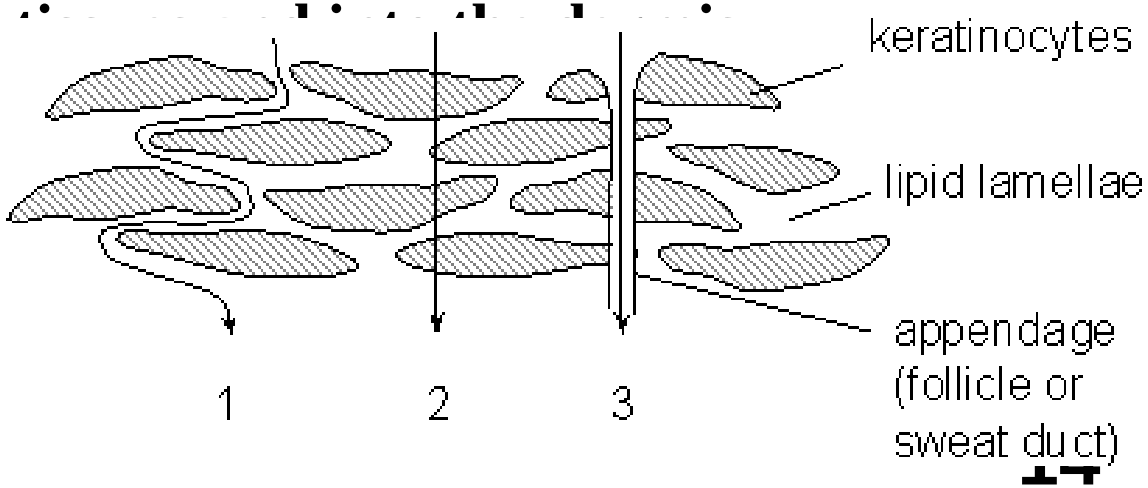
Disease treated	API
Keratolytic	Salicylic acid
Acne	Sulphur, Resorcinol
Antipruritic	Benzocaine, Menthol, Camphor
Emollient	Lanolin
Anti-inflammatory	Corticosteroid
Antifungal	Benzoic acid, Salicylic acid, miconazol, ketoconazole
Psoriasis	Coal tar



Stages In Percutaneous Absorption

Percutaneous drug absorption

- **Drugs can cross the skin barrier by three routes:**
  - **– Transcellular (across the cells)**
  - **– Paracellular (between the cells)**
  - **– Transappendageal (via hair follicles, sweat and sebum glands)**
- **Percutaneous drug absorption results from direct penetration through the stratum corneum, followed by passing through the epidermal**



Percutaneous drug absorption

- **It involves:-**
  - **Dissolution of the drug in the vehicle.**
  - **Diffusion of the solubilized drug from the vehicle to the surface of the skin.**
  - **Penetration of the drug through the layers of the skin principally stratum corneum.**

•The slowest step in percutaneous absorption usually involves passages through the stratum corneum

Properties that influence percutaneous absorption

A-biological factors:-

1. Skin age
2. Skin condition
3. Regional skin site
4. Special differences

B-Physicochemical factors:-

1. Drug skin / interactions (Skin hydration)
2. Drug / skin binding
3. Penetration enhancers
4. Drug / vehicle interactions (the choice of ointment base and formulation)
5. Type of oil

Biological factors:-

1. Skin age:

- It is assumed that the skin of the fetus, the young and the elderly are more permeable than the adult tissue.
- Children are more susceptible to the toxic effects of drugs and chemicals.

2-Skin condition:-

- The intact skin is a tough barrier but many agents damage it e.g. acids and alkalis injure barrier cells also cuts, abrasions and dermatitis.
- Solvents such as chloroform and methanol remove the lipid fraction and promote absorption.
- Solvents such as dimethylacetamide (DMA) and dimethylformamide (DMF) may be employed clinically to potentiate drug absorption.

Biological factors:-

3-Regional skin site:-

Variations in cutaneous permeability depend on the thickness and nature of stratum corneum.

Because of the relatively high permeability and the ease of access, the hyoscine transderm (T.T.S) employs to the post-auricular skin to insert drug percutaneously into the blood.

Here the layers of the stratum corneum are thinner and there is more sweat and sebaceous glands and many capillaries reach closer to the surface.

4-Special differences:-

The capillary blood supply and the sweating ability differ between humans

B-Physicochemical factors:-

1-Drug skin / interactions (Skin hydration)

When water saturates the skin, the tissue swells, softens and its permeability increases markedly. A compound which hydrates the skin could improve the treatment of dry, scaly dermatitis. These moisturizing agents include free fatty acids and urea.

Drug / skin binding

This may be important for sunscreens, for drugs such as topical steroids which form reservoirs in the stratum corneum and for the priming dose of the drugs released from the transderm system and other controlled release devices.

B-Physicochemical factors:-

2- Vehicle/ skin interactions

A pharmaceutical vehicle may

- **Change the physical state of skin**
- **Change inpermeability of the skin.**

It cause a hydration effect, or an alteration of skin temperature.

Oleaginous bases act as moisture barriers through which the sweat from the skin can not be passing, resulting in an increased hydration.

Vehicles of w/o emulsion type are probably next in effectiveness to oleaginous bases in enhancing the hydration of the skin.

w/o emulsions are more occlusive than o/w emulsions.

Commercial ointment products often contain humectants e.g. glycerol, propylene glycol or polyethylene glycol and emulsifiers which actually withdraw moisture from the skin.

3-Skin penetration enhancement

- **Examples of chemicals enhancing skin penetration of drugs:**
  - **Dimethylsulfoxide (DMSO)**
  - **Ethanol**
  - **Propylene glycol**
  - **Surfactants**
- **Mechanism of penetration enhancement:**
  - **Reduction of stratum corneum resistance**
  - **Alteration of hydration of stratum corneum**

4- Drug / vehicle interactions

- **In a disease condition such as eczema and dermatitis the release of the drug from the ointment will be the rate limiting factor and the skin functions as a sink.**
- **This may also happen when the drug diffusion in the vehicle is exceptionally slow.**
- **The release rate of the drug can be altered by changing drug concentration or the diffusion coefficient of the drug in the vehicle.**

6-Type of oil

The absorption of absorbable drugs is better from animal and vegetable oils than from mineral oils because the former types penetrate the skin more readily.

Factors affecting percutaneous absorption

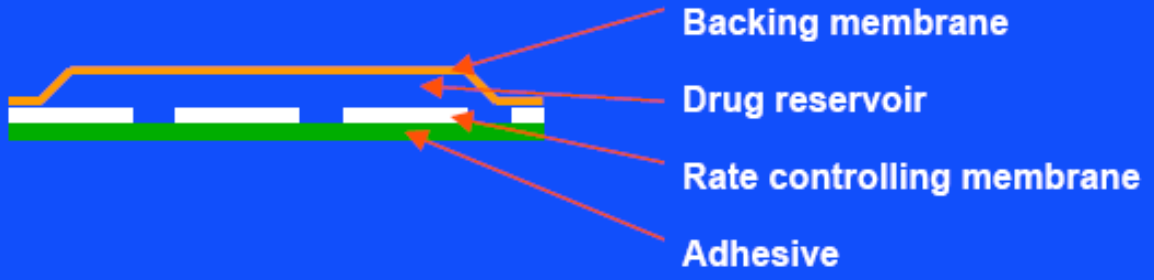
1. **Drug concentration - Increased concentration yields increased absorption, but not in direct linear proportion.**
2. **Surface area - Increased surface area yields increased absorption.**
3. **Physiochemical attraction to skin - Should be greater than attraction to vehicle.**
4. **Vehicle's tendency to cover skin and mix with sebum - enhanced contact with tissue cells for absorption.**

Factors affecting percutaneous absorption

5. **Increased hydration** Use of oleaginous vehicles and occlusives to trap sweat and increase absorption.
6. **Friction** -More rubbing / longer inunction yields greater absorption.
7. **Site of application** Better absorption through thin horny layer than thick or calloused skin.
8. **Contact time** Longer contact time generally allows more net absorption.
9. **Multiple-application** dosing Repeat application at same site to increase bioavailability and absorption.

Transdermal drug delivery systems

I. Reservoir type devices:



- Catapress DDS, Estraderm, Transderm Nitro, etc.
- Good when the stratum corneum is not the principal rate-limiting barrier for the diffusion of the drug
- Near constant-release rate
- Rupturing of the rate-limiting membrane may result in drug dumping
  - Other variations:
    - Multireservoir rate-limiting devices
    - Reservoir devices without rate-limiting membrane
      - a) Microencapsulated drug-reservoir type devices
      - b) Reservoir devices with solubility membranes

Advantages of TDDS

1. Avoids the chemically gastrointestinal (GI) problems
2. No GI distress or other physiological contraindications of the oral route
3. Can provide adequate absorption of certain drugs
4. Increased patient compliance
5. Avoids first-pass effect
6. Allows effective use of drugs with short biological half-lives
7. Allows administration of drugs with narrow therapeutic windows
8. Provides controlled plasma levels of very potent drugs
9. Drug input can be promptly interrupted when toxicity occurs

Disadvantages of TDDS

1. Drugs that require high blood levels cannot be administered
2. Adhesives may not adhere well to the types of skin
3. Drug or drug formulation may cause skin irritation or sensitization
4. Uncomfortable to wear
5. May not be economical

THEORY OF SEMISOLID DOSAGE FORMS

1- HYDROPHILIC PROPERTIES

2- RHEOLOGICAL PROPERTIES

3-DEGREE OF ABSORPTION

1- HYDROPHILIC PROPERTIES

- **The water absorbing capacity of oleaginous and water-in-oil bases may be expressed in terms of the water number**

- **Water number as the maximum quantity of water that is held (partly emulsified) by 100g of a base at 20^{o}C.**

- **The water absorbing capacity (water number)**
- **The test is carried by**

1. **Adding increments of water to the melted base and triturating until the mixture has cooled.**
2. **When no more water is absorbed, the product is placed in a refrigerator for several hours, removed, and allowed to come to room temperature.**
3. **The material is then rubbed on slab until water no larger exudes**
4. **finally, the amount of water remaining in the base is determined.**

2- RHEOLOGICAL PROPERTIES

Semisolids do not flow at low shear stresses but undergo reversible deformation like elastic solids.

When a characteristic shear stress, called the yield value or yield stress, is exceeded, they flow like liquids.

3-DEGRRE OF ABSORPTION

Generally, drug absorption into the skin occurs by passive diffusion. The rate of drug transport across the stratum corneum follows Fick's Law of Diffusion,

$da/dt = D.\Delta C.K /h$ Where:-

1. **dA/dt is the steady-state flux across stratum corneum**
2. **D is the diffusion coefficient or diffusivity of drug molecules**
3. **ΔC is the drug concentration gradient across the stratum corneum**
4. **K is the partition coefficient of the drug between skin and formulation medium**
5. **h is the thickness of the stratum corneum**

3-DEGRRE OF ABSORPTION

Transport of lipophilic drug molecules is facilitated by their dissolution into intercellular lipids around the cells of the stratum corneum.

Absorption of hydrophilic molecules into skin can occur through pores or openings of the hair follicles and sebaceous glands, but the relative surface area of these openings is barely 1% of the total skin surface. This small surface area limits the amount of drug absorption.

Formulation Factors for Semisolids

1-Dosage Form Viscosity (η)

- **Viscosity related to:**

Spreadability:

Increase viscosity lead to difficult in spreadability

Retention :

•Increase viscosity enhance the retention time of drug on the skin

Washability

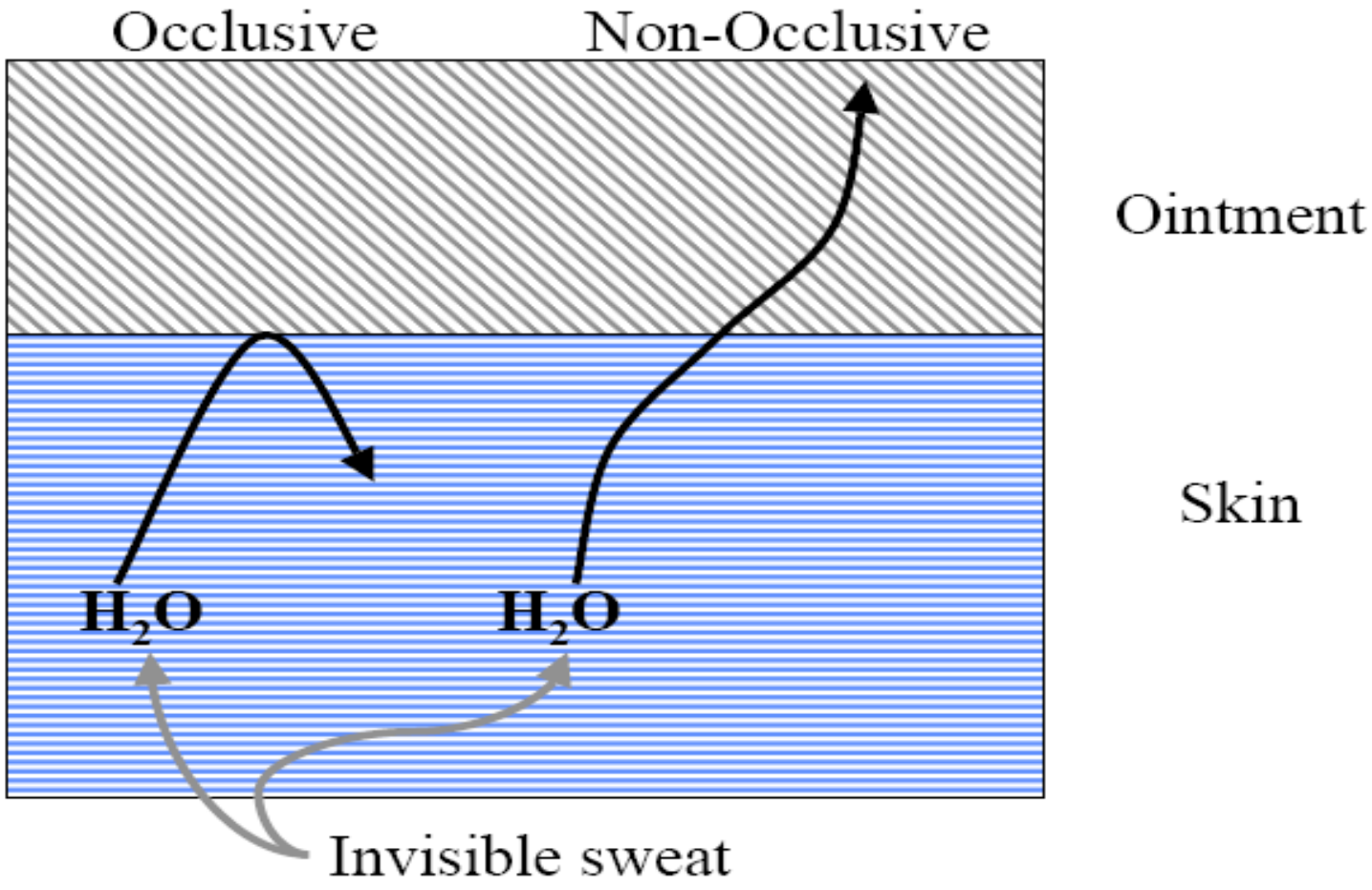
• highly viscous are harder to clean (poorly washable)

2- Occlusive vs Non(less)-occlusive

i.e. Water Permeability

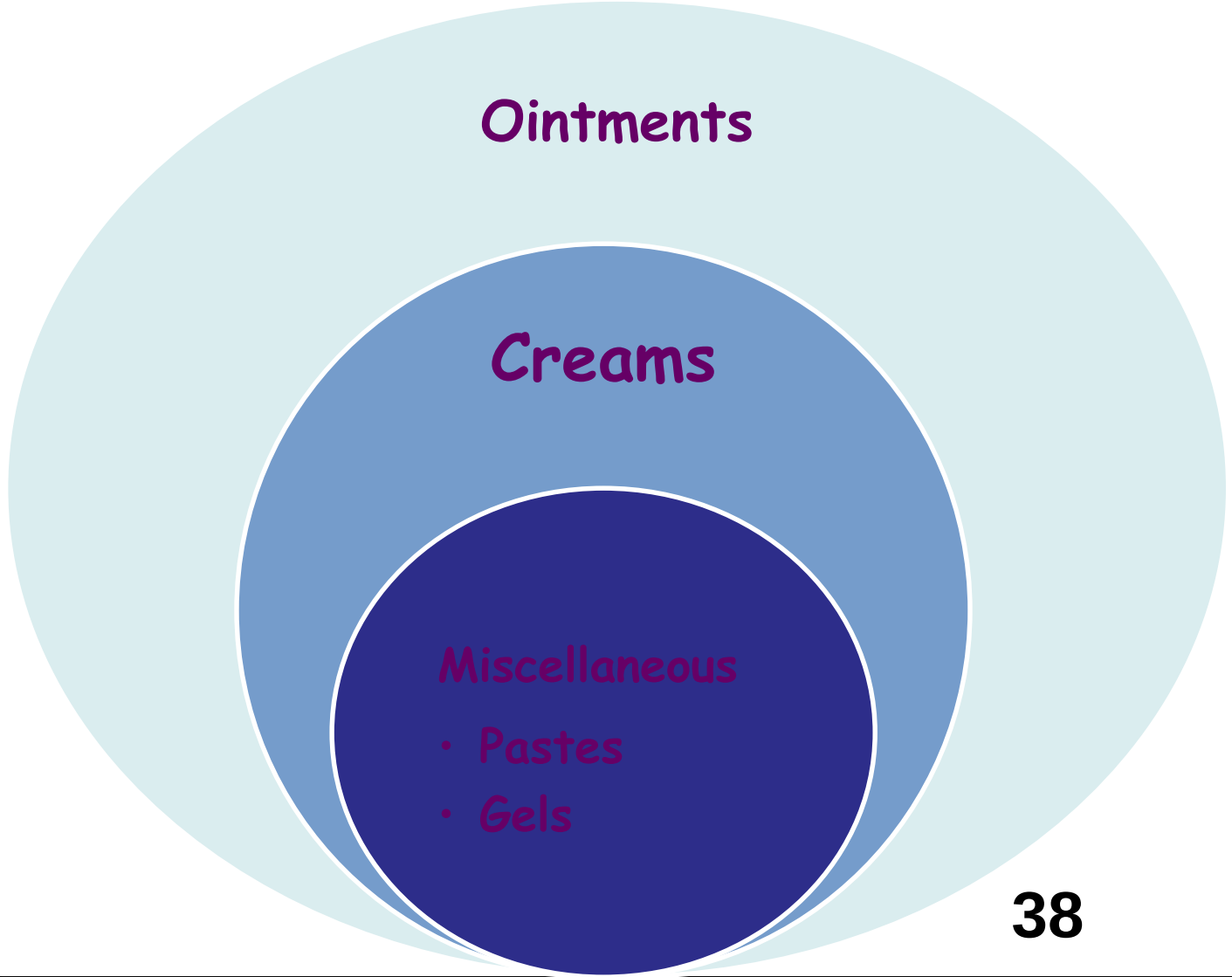
- Occlusive -> increase skin hydration
  - Good for dry skin
  - Bad for drying infection
- Enhance barrier
  - Good percutaneous absorption
  - Protection of skin
    - Example diaper rash
- Nature of vehicle determines what passes
  - Hydrophobic -> keeps H2O in
  - Hydrophilic -> H20 can pass

Occlusive and Skin Hydration



Skin Hydration ⇑ Permeability ⇑

Classification of semisolid dosage forms



Classification of semisolid dosage forms

Ointments:

Ointments are usually greasy preparation; the base is usually anhydrous and immiscible with skin secretions.

Creams:

Creams are traditionally O/W emulsions whilst *oily creams* are W/O emulsions.

Miscellaneous topicals

Pastes:

Pastes are vehicles (aqueous or oily) with a high concentration of highly powdered medicament.

Gels:

Gels (jellies) are usually transparent aqueous preparation.

OINTMENTS

•Ointments are greasy, semisolid preparation often anhydrous and containing dissolved or dispersed medicaments.

•Ointments are used topically for several purposes as

- **Protectants**
- **Antiseptics**
- **Emollients**
- **Antipruritics**
- **Kerotolytics**
- **Astringents.**

•In the case of a protective ointment, it serves to protect the skin against moisture, air, sun rays and other external factors.

Ointments Classified by the Base

1. **Hydrocarbon Bases**
2. **Absorption Bases**
3. **Water-Removable Bases (emulsion bases)**
   a) Water in oil emulsion bases (w/o)
   b) Oil in water emulsion bases(o/w)
4. **Water-Soluble Bases**

Selection of ointment base depends on following.

1. **Desired release rate** of the drug substance from the ointment base.
2. **Rate and extent** of topical or percutaneous drug absorption.
3. **Desirability of occlusion** of moisture from skin.
4. **Stability of the drug** in the ointment base.
5. Effect of **drug** on the **consistency** of base.
6. **Easy removal**

Hydrocarbons

- **Composition**
  - **– Mixture of hydrocarbons from petroleum**
  - **– Straight chained or branched**
  - **– C_{16} - C_{30} fluid hydrocarbons entrapped in matrix of C_{30} - C_{50}**
  - **– Single phase**

Hydrocarbon - Examples

- **Petrolatum**
  - **Yellow Petrolatum, Petroleum Jelly, Vaseline®**
  - **Melting range: 38°C - 60°C**
- **White Petrolatum**
  - **Purified and decolorized petrolatum**
  - **White Petrolatum Jelly, White Vaseline®**

Hydrocarbon - Examples Cont.

- **Yellow Ointment (Simple Ointment)**

  Petrolatum 95%

  Purified bees wax 5%

- **Mineral Oil**
  - **Mixture of liquid hydrocarbons**
  - **Levigating agent to incorporate solids**
  - **Maintains consistency from -15ºC to 60ºC**

Properties of Hydrocarbon Bases

1. Occlusive
2. Emollient
   - Hydrates skin due to sweat accumulation
   - Skin hydration keeps skin supple
3. Non-water washable
4. Hydrophobic
5. Greasy

Good base for water labile drugs

Example

- Bacitracin
- Tetracycline

Disadvantage

1. Greasy, difficult to remove from skin and clothing

Absorption Bases

- Named for water-absorbing properties
  - Can from W/O emulsion
  - Absorbs up to 3X weight in water
- Still retains semisolid viscosity
  - External phase oil -> occlusive

Hydrophilic Petrolatum USP

1. Cholesterol	30 gm
2. Stearyl Alcohol	30 gm
3. White Wax	80 gm
4. White Petrolatum	860 gm
Make to	1000 gm

- **Lanolin USP**
  - **Purified wax-like/fat-like substance from sheep wool**
- **Commercial Products:**
  - **Aquaphor® (Beirsdorf)**
  - **Polysorb® (Fougera)**

Absorption Base: Emulsified w/o Emulsion

1. **Lanolin USP (Anhydrous < 0.25% H20)**
2. **Lanolin (Hydrous)**
   - **USP Lanolin with 25 - 30% water**

Properties of Absorption Bases

Properties of Absorption Bases (Anhydrous)

Example:

Hydrophilic Petrolatum

- **Emollient**
- **Occlusive**
- **Absorbs water**
- **Anhydrous**
- **Greasy**

Properties of Emulsion Bases (W/O)

Example:

Lanolin, Cold Cream

- **Emollient**
- **Occlusive**
- **Contains water**
- **Absorb additional water**
- **Greasy**

Water-Removable Bases

- **O/W Emulsion**

- **Easy of removal with water**
- **Has better patient acceptance**

Hydrophilic Ointment USP XX

1. **Methylparaben 0.25**
2. **Propylparaben 0.15**
3. **Na lauryl sulfate 10.0**
4. **Propylene glycol 120.0**
5. **Stearyl alcohol 250.0**
6. **White petrolatum 250.0**
7. **Purified water 370.0**

Properties of Emulsion Bases (O/W)

- Water-washable, easier removal
- Non/Less-greasy
- Can be diluted with water
- Non/Less-occlusive
- Better cosmetic appearance
- All ingredients -> water soluble or washable
- Single phase

Water-Soluble Examples

- **Polyethylene Glycol Ointment (PEG)**
  - **Carbowax -> trade name PEG's MW > 100**
  - **Carbowax #'s --> approx MW --> η**
    - **1500, 1540, 4000, and 6000**
    - **1500 soft waxy solid**
    - **1540 like beeswax**
    - **6000 hard translucent waxy solid**
  - **Mix high and low MW to get properties wanted**
  - **Example --> Polyethylene Glycol Ointment**
    - **Polyethylene Glycol 3350.....400g**
    - **Polyethylene Glycol 400.....600g**

Properties of Water-Soluble Bases

- Usually anhydrous
- Water-soluble and washable
- Non-greasy
- Non-occlusive (less)
- Lipid-free
- Synthetic bases e.g. Carbowax
  - Nonvolatile & Inert (mostly)
  - Little hydrolysis, stable
  - Doesn't support mold growth
  - May dehydrate skin -> Hinders percutaneous absorption can sting mucosal membranes

	Hydrocarbon	Absorption	W/O Emulsion	O/W Emulsion	Water miscible
Composition	Oleaginous compounds	Oleaginous base + w/o surfactant	Oleaginous base + water (< 45% w/w) + w/o surfactant (HLB ≤8)	Oleaginous base + water (> 45% w/w) + o/w surfactant (HLB ≥9)	Polyethylene glycols (pegs)
Water content	Anhydrous	Anhydrous	Hydrous	Hydrous	Anhydrous, hydrous
Affinity for water	Hydrophobic	Hydrophilic	Hydrophilic	Hydrophilic	Hydrophilic
Spreadability	Difficult	Difficult	Moderate to easy	Easy	Moderate to easy
Washability	Non-washable	Non-washable	Non- or poorly washable	Washable	Washable
Stability	Oils poor; hydrocarbons better	Oils poor; hydrocarbons better	Unstable, especially alkali soaps and natural colloids	Unstable, especially alkali soaps and natural colloids; nonionics better	Stable
Drug incorporation potential	Solids or oils (oil soluble only)	Solids, oils, and aqueous solutions (small amounts)	Solids, oils, and aqueous solutions (small amounts)	Solid and aqueous solutions (small amounts)	Solid and aqueous solutions
Drug release potential*	Poor	Poor, but > oleaginous	Fair to good	Fair to good	Good
Occlusiveness	Yes	Yes	Sometimes	No	No
Uses	Protectants, emollients vehicles for hydrolysable drugs	Protestants, emollients vehicles for aqueous solutions, solids, and non-hydrolysable drugs	Emollients, cleansing creams, vehicles for solid, liquid, or non-hydrolysable drugs	Emollients, vehicles for solid, liquid, or non-hydrolysable drugs	Drug vehicles
Examples	White petrolatum, white ointment	Hydrophilic petrolatum, anhydrous lanolin, aquabase™, aquaphor®, polysorb®	Cold cream type, hydrous lanolin, hydrocream™, eucerin®, nivea®	Hydrophilic ointment, dermabase™, velvachol®, unibase®	PEG ointment, polybase™

Other additives for ointments

Antioxidants Such as

- **Butylated hydroxytoluene (BHT)**
- **Butylated hydroxyanisole (BHA)**
- **Chelating agents such as ethylenediaminetetra-cetic acid (EDTA).**

Preservatives

- **It is not required for anhydrous ointments because it is not favorable to the multiplications of any contaminating microorganisms.**
- **Ointments with an aqueous component require effective antimicrobial agents to prevent the growth of microorganisms.**
- **Those used most commonly are mixtures of hydroxybenzoate esters, sorbic acid and organic mercurials.**

Methods in making ointments

1. **Trituration**
2. **Fusion**
3. **Emulsification method**

GENERAL COMMENTS ABOUT COMPOUNDING OINTMENT BASES

1. **When melting a number of ingredients, melt the ingredient with the highest melting point first. Then gradually reduce the heat to melt the ingredient with the next lowest melting point.**
2. **The cooling step in an ointment's preparation is an important part of the compounding process.**
    1. **Do not accelerate the cooling process by putting the melt in water or ice. …….more stiff**
    2. **If adding volatile ingredients such as oils, flavors, or drugs, add them when the product is "cool to the back of the hand.”**

GENERAL COMMENTS ABOUT COMPOUNDING OINTMENT BASES

3. Ointments should be cooled until just a few degrees above solidification before they are poured into tubes or jars. They should be thick, viscous fluids. This will minimize "layering" of the ointment in the packaging container.

4. Most bases achieve their final consistency and texture several hours after they are compounded.

Trituration

- **Medicament is a solid insoluble in the base or a liquid present in small amount.**
- **Used to combine components of similar consistencies, all the base components are soft and fatty.**
- **Solid finely powdered and sieved to appropriate size.**
- **Use a mortar and pestle**

Fusion

- Ingredients are quite solid at room temperature
- Melt the ingredient with the highest melting point first
- Ingredients melted together and stirred to ensure homogeneity
- Small scale, use evaporating basin over a water-bath.

Fusion

- **Solids that are completely or partially soluble in the base, should be added in fine powder form to the molten base**
- **Liquid or semi-solid is added as the base is thickening e.g. methylsalicylate, coal tar solutions**
- **Insoluble solid, pass thru sieve and add as the base is thickening e.g. calamine, ZnO, starch**

The levigating agent

- **Should be chosen so that it is similar to the base being used. For example,**
  - **If an oleaginous base is being employed, mineral oil is satisfactory levigating agent.**
  - **If water- dispersible base is being used, glycerin is a suitable levigating agent.**

Emulsification Method:

- Used when some of the ointment components are of aqueous nature and others are of fatty nature, sometimes the medicament as well is soluble in water.
- All the fatty compounds are added and melted together, stirred till a uniform mixture is obtained.
- All the water soluble compounds are dissolved in water (sometimes including the drug itself), then the solution is heated roughly to the same temperature as the hot fatty mixture or higher.
- Then the two portions are mixed and stirred vigorously till the product sets.

Lectures on Creams

1. Introduction
2. Types of creams
3. Mode of action
4. Factors influencing efficacy
5. Formulation

Creams

- a viscous, semisolid emulsion of oil, e.g. lanolin or petrolatum, and water, the main ingredient being water
- Preferable – spreads readily, less greasy, soothing.
- oil and water remain well mixed by adding emulsifying agents
  - Oily cream (water-in-oil) - emollient & cleansing
  - Non-greasy aqueous cream (oil-in-water) - most useful as water washable bases
- a large number of topical drugs are manufactured in a cream base, e.g. hydrocortisone cream

•**Oil-in-water creams are more comfortable and cosmetically acceptable as they are less greasy and more easily washed off using water.**

•**Water-in-oil creams are more difficult to handle but many drugs which are incorporated into creams are hydrophobic and will be released more readily from a water-in-oil cream than an oil-in-water cream.**

•**Water-in-oil creams are also more moisturising as they provide an oily barrier which reduces water loss from the stratum corneum, the outmost layer of the skin.**

•**Creams are susceptible to microbial growth.**

Factors influencing efficacy

- **Diffusion through skin**
  - **Partition coefficient, pH, solubility….at the various layers of the skin**
  - **Surfactants**
- **Factors influencing absorption**
  - **Age, skin condition, drug/skin/vehicle interactions, temperature……**

- **Water phase evaporates leaving thin film**
- **Doesn't cover hole surface -> Not as occlusive**

- **Moisturizers added to replace skin**
- **H2O evaporation concentrates drug on skin surface**

General compounding procedure for creams

- **Emulsified creams are prepared by**
  - **Heating the components of the oily phase until melt**
  - **And then cooling to 60°C.**
  - **The components of the aqueous phase are mixed in a separate vessel and also heated to60°c.**
  - **The aqueous phase then added to the oily phase at same temperature gradually with constant stirring until cool.**
  - **Rapid cooling may result in separation of high melting point components.**

Examples of Creams

e.g. Aqueous cream BP

30% of emulsifying ointment with purified water preserved with chlorocresol.

- **Boil and cool sufficient purified water. Measure the quantity required and dissolve the chlorocresol with the aid of gentle heat.**
- **Add solution to the melted emulsifying ointment. Stir gently until cold.**

Oily cream (hydrous ointment) BP

- **Wool alcohol ointment** **500g**
- **Phenoxyethanol** **10g**
- **Dried mag. Sulfate** **5g**
- **Purified water** **485g**

wool alcohol ointment

- **Hard paraffin**
- **Liquid paraffin**
- **Wool alcohol**
- **Yellow or white soft paraffin**

Pastes

Pastes are ointments containing high proportion of fine powder, such as starch, dextrin, zinc oxide, sulfur, calcium carbonate, talc or other medicinal substances of an astringent, antiseptic, or protective nature.

Pastes

- **Pastes differ from ointments in the following:**

1. **Fatty pastes contain as much as 50% of powders with soft fat or as much as 70% of powders with less viscous oils as the vehicle. So, they are stiffer than ointment.**
2. **Medicaments incorporated in the pastes are absorbed less readily than from ointment i.e. having more superficial action, but giving better protection (epidermic).**
3. **Are not suitable for application to hairy parts like scalp, as they will form a dense mass.**
4. **Don't melt at body temperature.**

Types of pastes

1. **Ointment- like:- preparations containing the above mentioned powders with liquid petrolatum, white petrolatum, wool fat, white wax, and other fats which are medicated with salicylic acid, acetylsalicylic acid, eugenol and Peruvian balsam.**

2. **Jelly pastes: containing glycerin with starch, glycerogelatin or other water soluble gels such as pectin and tragacanth.**

Examples of pastes

Gelatin of zinc paste, E.P. Unna's paste

Zinc oxide	15 g
Gelatin	15g
Glycerin	35g
Distilled water ad to	100g

Zinc Oxide Paste USP (Lasser's plain Zinc Paste)

Zinc Oxide	25%
Starch	25%
White Petrolatum	50%

Gels or Jellies

- Gels are semisolid dosage form for topical or other local use.
- Usually transparent or translucent and have a variety of uses.
- Spermicides and lubricants are often presented as gels.
- Preparation containing coal tar or other drugs used for treatment of psoriasis and eczema also presented in this form.
- Slightly more viscous gels are used as lubricants for catheter, examination gloves and surgical instruments.

Ingredients for preparing ointments and creams

1. Oil
2. Thickners
3. Emulsifier
4. Water
5. Antioxidants
6. Preservatives

Oil

- **Almond oil is very best for face creams.**
- **For healing the skin olive oil is perfect because it heals by itself.**
- **For dry skin sunflower oil is very good.**
- **Sesame oil is a nourishing oil and it protects a little bit against too much sun.**

Thickener

- **Thickeners are all substances that make a cream or ointment out of the liquid oil and water**
  - **Beeswax, good protection, a film stays on the skin. Strong thickening.**
  - **Cocoa butter, made from cocoa beans, Soft thickening.**
  - **Wool fat (lanolin), made from the wool of sheeps. Very soft but healing effects. Is a soft emulsifier. Soft thickening.**
  - **Cetyl alcohol, a substance similar to skin substances. White and not greasy. Stabilizes emulsions. Very strong thickening.**

1. **Emulsifier**
   - **Cetyl and stearyl alcohol**
2. **Antioxidants (Vegetable oils may become rancid due to oxidation)**
   - **BHA &BHT**
3. **Preservatives (for creams due to high water content)**

PACKAGING OF SEMISOLIDS

- Most semisolid products are manufacture by heating and are filled into the container while cooling still in the liquid state.
- It is important to established optimum pour point, the best temperature for filling and set or congealing point, the temperature at which the product become immobile in the container.
- Topical dermatological products are packed in either jar or tubes whereas ophthalmic, nasal, vaginal and rectal semisolid products are almost always packed in tubes.

PACKAGING OF SEMISOLIDS

- **Container closures and other component part of drug packages, to be suitable for that intended use must not be:-**
  - **Reactive**
  - **Absorptive**

  to the extent that affect identity, strength, quality or purity of drug.

PACKAGING OF SEMISOLIDS

- Ointment jars are made up of clear or opaque glass or plastic.
- Some are colored green, amber or blue.
- Opaque jars are used for light sensitive products, are porcelain white, dark green or amber.
- Tubes use to package topical pharmaceutical products are gaining in popularity since they are they are light in weight, relatively inexpensive, convenient for use, compatible with most formulative component and provide protection against external contamination

PACKAGING OF SEMISOLIDS

- Ointment tubes are made of aluminum or plastic.
- When the ointment is use for ophthalmic, rectal, vaginal or nasal application, they are packed with special applicator tips.
- Ointment, creams and gels are most frequently packed in 5, 15 and 30 gm tubes.
- Ophthalmic ointments typically are packed in small aluminum or collapsible plastic tubes holding 3.5 gm of ointment

PACKAGING OF SEMISOLIDS

- The mouth of jar should be covered with a grease proof-paper disc.
- Containers should be well filled and airtight to prevent evaporation.

Packaging And Stability :

- **The immediate container and closure are particularly important in affecting product stability.**

Packaging And Stability:

■ Glass

- Glass is resistant to chemical and physical change and is the most commonly used material.

Limitations	Overcome
1. Its alkaline surface	use of Borosilicate glass
2. Ions may precipitate insoluble crystals from the glass	the use of buffers
3- Permits the transmission of light which may accelerate decomposition.	Amber coloured glass

Packaging And Stability :

- **Plastics**

The problems with plastic are:

1. **Migration of the drug through the plastic into the environment.**
2. **Transfer of environmental moisture, oxygen, and other elements into the pharmaceutical product.**
3. **Leaching of container ingredients into the drug.**
4. **Adsorption of the active drug or excipients by the plastic.**

Packaging And Stability :

- **Metals**

- **Various alloys and aluminium tubes may be utilized as containers for emulsions, ointments, creams and pastes.**

- **Limitation: They may cause corrosion and precipitation in the drug product.**

- **Overcome: Coating the tubes with polymers may reduce these tendencies.**

Packaging And Stability :

- **Rubber**

- **Rubber also has the problems of extraction of drug ingredients and leaching of container ingredients.**

- **The pretreatment of rubber vial stoppers and closures with water and steam reduces potential leaching.**

QUALITY ASSURANCE AND QUALITY CONTROL OF SEMISOLIDS

A-IN PROCESS CONTROL

- **Processing of semisolids involves mixing, milling, heating and cooling of bulk products. Therefore, it is essential to develop in process control.**
  1. **Complete solubilization (if applicable)**
  2. **pH**
  3. **Viscosity measurement**
  4. **Uniformity of distribution of active ingredients**
  5. **Physical stability**
  6. **Measurement of density or specific gravity.**

B- FINISHED PRODUCT SPECIFICATIONS

1. **Microbial test**
2. **Physical tests**
    1. **Viscosity measurement**
    2. **Texture analysis:- Texture analyzer is used to detect,**
        - **a)Ointment flow characteristic**
        - **b)Ointment consistency**
3. **Chemical tests**
    - **a.Chemical potency test**
    - **b.Content uniformity test**
    - **C-pH measurement**
4. **In-vitro release profile test**